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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HARRIS, ALANA M	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 04/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/965,796	GOLDENBERG, DAVID M.	
	Examiner	Art Unit	
	Alana M. Harris, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *29 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-97* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-97* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/01/01*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I (claims 24-59) in the reply filed on October 29, 2004 is acknowledged. The Examiner has reconsidered the election/restriction requirement mailed September 29, 2004 and has eliminated the restriction between the two groups and will examine all claims (claims 24-97).

2. Claims 24-97 are pending.

Claims 1-23 were cancelled.

Claims 24-97 are examined on the merits.

Information Disclosure Statement

3. Applicant submitted an Information Disclosure Statement (IDS) on October 1, 2001 noting that the listed documents were submitted in parent application serial number 09/307,816 filed May 10, 1999. The Examiner has reviewed the parent application, as well as most of the documents therein. References A10, A12, A17 and A19 were not in the parent application and consequently were not reviewed. Moreover, it is not clear if references A12, A17 and A19 have the proper title and corresponding journal listing. Applicant is respectfully requested to supply these references. Likewise, Applicant is requested to review the source of the documents and note all pertinent information. The Examiner has corrected several citations with the proper date of publication, page numbers and matching of publication with corresponding journal.

Reference A21 was added to the IDS by the Examiner because the journal citation listed for reference A19 actual corresponded to an article by Krietman and not Vuist et al. Applicant is requested to review the IDS and the changes made by the Examiner.

Specification

4. The instant application does not properly reflect the current status of the parent application in the first line of the specification. U.S. application serial number 09/307,816 filed May 10, 1999 is now U.S. Patent 6,306,393. The first line of the specification does not list the provisional application, nor the U.S. application from which the current application is a continuation-in-part. Applicants are requested to review the first line of the specification and include all pertinent and proper information.

5. The use of the trademarks, PROLEUKIN ®, TECELEUKIN ® and ACTIMMUNE ® have been noted in this application, see bridging sentence of pages 27 and 28. It should be capitalized wherever it appears and be accompanied by the generic terminology. Applicants are requested to review the entire application for other trademarks.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 24-97 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for human, humanized or chimeric anti-CD22 antibodies, does not reasonably provide enablement for fragments thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

It is well established in the art that the formation of an intact antigen-binding site generally requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs which provide the majority of the contact residues for the binding of the antibody to its target epitope. The amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity, which is characteristic of the parent immunoglobulin. It is expected that all of the heavy and light chain CDRs in their proper order and in the context of framework sequences which maintain their required conformation, are required in order to produce a protein having antigen-binding function and that proper association of heavy and light chain variable regions is required in order to form functional antigen binding sites. Even minor changes in the amino acid sequences of the heavy and light variable regions,

particularly in the CDRs, may dramatically affect antigen-binding function as evidenced by Rudikoff et al (Proc Natl Acad Sci USA 79: 1979-1983, March 1982). Rudikoff teaches that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding function. It is unlikely that the fragments listed in the claims which contain less than the full complement of CDRs from the heavy and light chain variable regions of an anti-CD22 or any other antibody listed in the claims (i.e. anti-CD19, anti-CD20, anti-CD52and anti-CD74) in unspecified order and fused to any human or nonhuman framework sequence, have the required binding function.

The specification provides no direction or guidance regarding how to produce fusion proteins and antibodies as broadly defined by the claims. Undue experimentation would be required to produce the invention commensurate with the scope of the claims from the written disclosure alone.

Further, a fragment of the heavy chain can be any one of the constant regions (CH1-3) and also may be the hinge region. However, the language also reads on small amino acid sequences, which are incomplete regions of the constant region of the antibody. There is no support in the specification for linking the variable region to any or the entire myriad "fragments" which are encompassed within this language. One of skill in the art would neither expect nor predict the appropriate functioning of the antibody as broadly as is claimed. It is suggested that the specific portion of the human constant region, which the variable region is covalently linked to, be explicitly recited within the claim or this language be removed completely in order to obviate this rejection.

Therefore, in view of the lack of guidance in the specification and in view of the discussion above one of skill in the art would be required to perform undue experimentation in order to practice the claimed invention.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 60-97 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. The recitation "...agent is attached *indirectly* to the ...antibody..." 60-62, 85 and 86 is indefinite. It is apparent Applicant is contrasting how an agent is bound to the antibody, however it is not clear what indirectly means. It is not clear if indirectly means the agent arbitrarily attaches to the any residue on the protein, is set upon the antibody or attaches through some other linkage. Applicant is requested to clarify the term "indirectly" as it relates to the attachment of the agent to the antibody.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

11. Claims 24-26, 28, 29, 31, 32, 36-38, 44-46, 49, 51, 52, 55-57, 60-70, 73-77, 79 and 90-93 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent number 5,789,554 (filed July 31, 1996). U.S. Patent number 5,789,554 discloses "[c]onjugates of chimeric and humanized chimeric LL2 antibodies with cytotoxic agents or labels... use[d] in therapy... of B-cell lymphomas and leukemias", see last sentence of the Abstract and column 2, lines 56-62. It is art known that LL2 antibodies are anti-CD22 monoclonal antibodies. The patent reveals the implementation of fragments from both human and murine immunoglobulin chains in methods of treatment, see column 2, lines 37-50; column 2, line 65-column 3, line 15.

These antibodies of the disclosed method could be attached to cytotoxic agents, as well as chemotherapeutic drugs, chelators, fluorescent molecules, radionuclides or toxins, see column 5, lines 20-29; Example 9 of columns 19 and 20. The disclosed

antibodies can be conjugated to a radioisotope other than ^{131}I for example ^{90}Y or ^{111}In using a chelating agent, see column 20, lines 35-42.

12. Claims 24-26, 28, 29, 31, 32, 36-38, 44-46, 49, 51, 52, 55-57, 60-70, 73-77, 79 and 90-93 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 96/04925 (22 February 1996/ IDS reference A8). The WO document discloses immunoconjugates comprising chimeric and humanized LL2 antibodies with cytotoxic agents or labels for use in therapy of B-cell lymphomas and leukemias, see Abstract and page 1, lines 5-12; page 3, line 31-page 4, line 13; page 7, lines 27-38. The document reveals the implementation of fragments from both human and murine immunoglobulin chains in methods of treatment, see page 3, line 24-page 4, line 5; page 4, lines 14-32. A wide variety of diagnostic and therapeutic reagents can be conjugated to the disclosed antibodies such as doxorubicin, taxol, chelators, detectable labels such as fluorescent molecules, cytotoxic agents such as heavy metals or radionucleoides and toxins such as *Pseudomonas* exotoxin, see page 8, lines 17-26; page 33, lines 3-11; and page 33, line 33-page 34, line 10. The disclosed antibodies can be conjugated to a radioisotope other than ^{131}I for example ^{90}Y or ^{111}In using a chelating agent, see page 34, lines 3-10.

13. Claims 60-65, 67-69 and 90-95 are rejected under 35 U.S.C. 102(b) as being anticipated by Juweid et al. (Cancer Research (Suppl.) 55:5899s-5907s, December 1, 1995/ IDS reference A20). Juweid discloses "[t]reatment of Non-Hodgkin's lymphoma

with radiolabeled murine, chimeric [and] humanized LL2, an anti-CD22 monoclonal antibody, see title and entire article. The monoclonal antibodies were radiolabeled with ^{131}I and prednisone was administered in one particular case and intrathecal chemotherapy and EPOCH chemotherapeutic regimen was administered in others, see page 5902s, column 1, middle of paragraph and column 2, "Initial Therapeutic..." section; and bridging sentence of pages 5902s and 5903s. Juweid also discloses the preparation and radiolabeling of the naked antibody on pate 5900s, column 1, in the "Preparation..." section. The cumulative radioactive dose administered to patients ranged from 15.1 mCi ^{131}I-LL2 IgG to 343 mCi ^{131}I-LL2 $F(ab')_2$, which is within the range of 15 to 40 mCi stated by Applicant.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. Claims 24-26, 28, 29, 31, 32, 36-38, 44-47, 49, 51, 52, 55, 56, 60-69, 73-77 and 90-93 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent number 5,789,554 (filed July 31, 1996), and in view of Li et al. (Cellular Immunology 118: 85-99, 1989). The teachings of patent #5,789,554 have been presented in the

102(e) rejection. U.S. Patent '554 does not teach a therapeutic composition comprising at least two monoclonal antibodies that bind distinct CD22 epitopes.

However, Li teaches that four anti-CD22 monoclonal antibodies, UV22-1, UV22-2, HD6 and RFB47 recognize CD22 A and B epitopes. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to administer a combination of antibodies, to different CD22 epitopes, as taught in the Li reference in the method of treating B cell malignancies, as taught in the patent. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by teachings in the Li reference, that a mixture of antibodies to the different epitopes of CD-22 would be a more efficacious in therapeutic methods, as well as enhance the treatment modality.

16. Claims 24-29, 31, 32, 36-38, 44-46, 49, 51, 52, 55-57, 60-70, 73-77 and 90-93 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent number 5,789,554 (filed July 31, 1996), and further in view of U.S. Patent number 5,106,955 (April 21, 1992). The teachings of patent #5,789,554 have been presented in the 102(e) rejection. U.S. Patent '554 does not teach a therapeutic composition comprising the chemotherapeutic drugs, a nitrosourea derivative, hormones and an antiviral toxin linked via crosslinking agents.

However, U.S. patent #5,106,995 teaches the specific chemotherapeutic drugs, nitrosourea and hormones and antiviral toxins, see entire page with columns 5 and 6. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the

claimed invention was made to administer a therapeutic combination of a known anticancer antibody with other anticancer molecules in the method of treating B cell malignancies, as taught in both patents. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by teachings in the patents that conjugates of anti-CD22 antibodies with anticancer agents are efficacious in the treatment of B-cell lymphomas and leukemias, see patent '554, abstract and Example 9 of columns 19 and 20; see patent '955, abstract and columns 5 and 6.

17. Claims 24-26, 28, 29, 31, 32, 36-42, 44-46, 48, 49, 51, 52, 55-57, 60-70, 73-77 and 90-93 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent number 5,789,554 (filed July 31, 1996), in view of U.S. Patent Number 5,686,072 (filed February 22, 1994/ IDS reference A1) and WO 95/09917 (April 13, 1995/ IDS reference A5). The teaching of patent '554, a method of treating B cell lymphomas comprising the administration of anti-CD22 antibodies has been previously discussed. The patent does not teach a multivalent fusion protein that additionally comprises at least one antibody component that binds with CD19 or a trivalent, tetravalent or quintavalent fusion.

However, U.S. patent #5,686,072 teaches the administration of an unconjugated anti-CD19 antibody (also regarded as a naked antibody), toxins (ricin, diptheria toxins in a mixture with anti-CD22 for the immunotherapeutic treatment of cancer, see abstract. It would have *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to combine an anti-CD19 antibody with an anti-CD22 antibody as taught in patent '072 . One of ordinary skill in the art would have been

motivated to do so with a reasonable expectation of success by the teachings of both patents that the co-administration of anti-CD19 and anti-CD22 antibodies appears to provide a synergistic and advantageous cancer treatment, see both patents.

The WO document teaches that recombinant bispecific tetravalent antibodies are useful in both therapeutic and immunodiagnostic applications and can be produced with relative ease.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of claimed invention to produce a tetravalent construct comprising anti-CD22 antibodies, as well as trivalent and quintavalent fusion proteins. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by teachings in both patents and the WO document that tetravalent antibody constructs are more effective than monoclonal antibody to effectively target more antigenic sites on the cancer cells and to advantageously increase the avidity of antigen binding.

18. Claims 24-26, 28, 29, 31, 32, 34-39, 44-46, 48, 49, 51, 52, 55-57, 60-70, 73-77 and 90-93 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent number 5,789,554 (filed July 31, 1996), in view of European Patent Application 0 510 949 A2 (October 28, 1992/ IDS reference A4). The teaching of patent '554, a method of treating B cell lymphomas comprising the administration of anti-CD22 antibodies has been previously discussed. The patent does not teach a therapeutic composition comprising the said anti-CD22 antibody and an immunomodulator, such as an additional antibody component and toxins.

However, EP 0 510 949 A2 teaches conjugate formulas comprising two moieties, wherein both have physiological activity, see column 3, lines 3-6. The moieties may be an antibody and fragments thereof, interleukins 1-10, molecules that bind CD19 (regarded by the Examiner as an antibody), growth factors, GM-CSF, G-CSF and toxins (i.e., ricin, diptheria toxins) in a mixture with anti-CD22 for the immunotherapeutic treatment of cancer, see abstract and column 3, lines 24-47. It would have *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to combine efficacious anti-tumor agents within an anti-cancer therapeutic composition. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of both patents that such conjugate compositions provide a synergistic and advantageous cancer treatment, see both patents.

19. Claims 24-38, 43-46, 49, 51, 52 and 55-97 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent number 5,789,554 (filed July 31, 1996), and further in view of U.S. Patent number 5,698,178 (filed April 8, 1998). The teachings of patent #5,789,554 have been presented in the 102(e) rejection. U.S. Patent '554 does not teach a therapeutic composition comprising a chemotherapeutic drug, immunomodulator, antiviral drugs, radioisotope, boron addend, anti-bacterial drug and photoactive agent or dye, as well as specific modes of attaching these molecules. Moreover, patent '554 does not teach the administration of the immunoconjugate

comprising an anti-CD22 antibody with radioisotopes iodine and yttrium in the specific dosages set forth in claims 94-97.

However, U.S. patent #5,698,178 teaches specific radioisotopes, ^{198}Au, ^{32}P, ^{125}I, ^{90}Y, ^{186}Re, ^{188}Re, ^{67}Cu and ^{211}At; toxins, ricin A-chain, *Psuedomonas* endotoxin, gelonin, ribonuclease, abrin, and pokeweed antiviral protein; chemotherapeutic drugs, nitrogen msutards, alkyl sulfonates, nitrosoureas, triazenses, folic acid analogs, antiboitics, platinum coordination complexes, hormones, pyrimidine analogs; boron addends, such as carboranes; and immunomodulators, granulocyte-colony stimulating factor (G-CSF), GM-CSF, IL-1 and IL-3, see , see column 4, lines 35-56; column 6, lines 15-19; column 8, lines 26-36; column 16, line 59-column 17, line 2; column 23, line 11-column 24, line 6; column 31, lines 34-37. The patent also teaches the use of fluorescent chromogens or dyes, such as porphyrins in therapy termed photoradiation or photodynamic therapy in order to destroy a tumor population, see column 24, lines 7-31, 45-54. Patent '178 also teaches modes of attaching the therapeutic agents to the antibodies and antibody fragments, $F(ab')_2$, $F(ab)_2$, Fab' and Fab via chelators such as ethylenediaminetetraacetic acid , DPTA, polyethyleneglycol, TETA and a carrier polymer such as aminodextran, see column 15, lines 56-67; column 17, lines 57-67; column 20, lines 28-34; and column 23, lines 19-31. Attachment of therapeutic agents to anti-CD22 antibodies may be implemented via a free sulfhydryl group, see column 14, lines 28-38 and column 17, lines 57-67. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to administer

a therapeutic combination of a known anticancer antibody with other anticancer molecules in the method of B cell treatment.

Additionally, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to administer the naked anti-CD22 antibody in the recited dosages. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by teachings well known in the art, that dosages of any pharmaceutical composition must be adjusted and optimized.

20. Claims 24-38, 43-46, 49, 51, 52 and 55-97 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 96/04925 (22 February 1996/ IDS reference A8), and further in view of U.S. Patent number 5,698,178 (filed April 8, 1998). The teachings of the WO document have been presented in the 102(b) rejection. U.S. Patent '554 does not teach a therapeutic composition comprising a chemotherapeutic drug, immunomodulator, antiviral drugs, radioisotope, boron addend, anti-bacterial drug and photoactive agent or dye, as well as specific modes of attaching these molecules. Moreover, WO document 96/04925 does not teach the administration of the immunoconjugate comprising an anti-CD22 antibody with radioisotopes iodine and yttrium in the specific dosages set forth in claims 94-97.

However, U.S. patent #5,698,178 teaches specific radioisotopes, ^{198}Au, ^{32}P, ^{125}I, ^{90}Y, ^{186}Re, ^{188}Re, ^{67}Cu and ^{211}At; toxins, ricin A-chain, *Psuedomonas* endotoxin, gelonin, ribonuclease, abrin, and pokeweed antiviral protein; chemotherapeutic drugs, nitrogen msutards, alkyl sulfonates, nitrosoureas, triazenses, folic acid analogs,

antiboitics, platinum coordination complexes, hormones, pyrimidine analogs; boron addends, such as carboranes; and immunomodulators, granulocyte-colony stimulating factor (G-CSF), GM-CSF, IL-1 and IL-3, see , see column 4, lines 35-56; column 6, lines 15-19; column 8, lines 26-36; column 16, line 59-column 17, line 2; column 23, line 11-column 24, line 6; column 31, lines 34-37. The patent also teaches the use of fluorescent chromogens or dyes, such as porphyrins in therapy termed photoradiation or photodynamic therapy in order to destroy a tumor population, see column 24, lines 7-31, 45-54. Patent '178 also teaches modes of attaching the therapeutic agents to the antibodies and antibody fragments, $F(ab')_2$, $F(ab)_2$, Fab' and Fab via chelators such as ethylenediaminetetraacetic acid, DPTA, polyethyleneglycol, TETA and a carrier polymer such as aminodextran, see column 15, lines 56-67; column 17, lines 57-67; column 20, lines 28-34; and column 23, lines 19-31. Attachment of therapeutic agents to anti-CD22 antibodies may be implemented via a free sulfhydryl group, see column 14, lines 28-38 and column 17, lines 57-67. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to combine the teachings of both documents to administer a therapeutic combination of a known anticancer antibody with other anticancer molecules in the method of B cell treatment.

Additionally, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to administer the naked anti-CD22 antibody in the recited dosages. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by teachings well known in

the art, that dosages of any pharmaceutical composition must be adjusted and optimized.

21. Claims 60-97 are rejected under 35 U.S.C. 103(a) as being unpatentable over Juweid et al. (Cancer Research (Suppl.) 55:5899s-5907s, December 1, 1995/ IDS reference A20), in view of U.S. Patent number 5,698,178 (filed April 8, 1998). The teachings of Juweid have been presented in the 102(b) rejected listed in paragraph 13. Juweid does not teach wherein the therapeutic agent is ^{90}Y or ^{67}Cu attached via a free sulfhydrl group or by means of an aminodextran and the chelating agents are DPTA and TETA. Juweid also does not teach does not teach the administration of the immunoconjugate comprising an anti-CD22 antibody with radioisotopes iodine and yttrium in the specific dosages set forth in claims 94-97.

However, U.S. patent #5,698,178 teaches specific radioisotopes, ^{198}Au, ^{32}P, ^{125}I, ^{90}Y, ^{186}Re, ^{188}Re, ^{67}Cu and ^{211}At; toxins, ricin A-chain, *Psuedomonas* endotoxin, gelonin, ribonuclease, abrin, and pokeweed antiviral protein; chemotherapeutic drugs, nitrogen msutards, alkyl sulfonates, nitrosoureas, triazenses, folic acid analogs, antiboitics, platinum coordination complexes, hormones, pyrimidine analogs; boron addends, such as carboranes; and immunomodulators, granulocyte-colony stimulating factor (G-CSF), GM-CSF, IL-1 and IL-3, see , see column 4, lines 35-56; column 6, lines 15-19; column 8, lines 26-36; column 16, line 59-column 17, line 2; column 23, line 11-column 24, line 6; column 31, lines 34-37. The patent also teaches the use of fluorescent chromogens or dyes, such as porphyrins in therapy termed photoradiation or photodynamic therapy in order to destroy a tumor population, see column 24, lines 7-

31, 45-54. Patent '178 also teaches modes of attaching the therapeutic agents to the antibodies and antibody fragments, $F(ab')_2$, $F(ab)_2$, Fab' and Fab via chelators such as ethylenediaminetetraacetic acid , DPTA, polyethyleneglycol , TETA and a carrier polymer such as aminodextran, see column 15, lines 56-67; column 17, lines 57-67; column 20, lines 28-34; and column 23, lines 19-31. Attachment of therapeutic agents to anti-CD22 antibodies may be implemented via a free sulfhydryl group, see column 14, lines 28-38 and column 17, lines 57-67. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to combine the teachings of both documents to administer a therapeutic combination of a known anticancer antibody with other anticancer molecules in the method of B cell treatment.

Additionally, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to administer the naked anti-CD22 antibody in the recited dosages. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by teachings well known in the art, that dosages of any pharmaceutical composition must be adjusted and optimized.

Double Patenting

22. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

23. Claims 24-97 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 24-44 of copending Application No. 10/314,330 (filed December 9, 2002). Although the conflicting claims are not identical, they are not patentably distinct from each other because the methods claims of both applications are directed toward treating a B-cell malignancy comprising administering an anti-CD22 antibody with an additional therapeutic agent, such as an additional antibody, chemotherapeutic agent, radiolabel or cytokine.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

24. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (571)272-0831. The examiner works a flexible schedule, however she can normally be reached between the hours of 6:30 am to 5:30 pm, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER

Alana M. Harris, Ph.D.
04 January 2004